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T.R.L.R. 27
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Project: A 10.2

By authority of
C.O., CWS Tech. Comd.

A Memorandum Report

UNCLASSIFIED

Inf. CYANOGEN CHLORIDE (Cl)

LC 50 FOR RATS: 2 MIN. EXPOSURE

By

I. Fuhr

E. H. Krackow

DECLASSIFIED
DOD DIR 5200.9

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Info. Div., CWS Tech. Comd., S.A.
12 April 1944

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CYANOGEN CHLORIDE

LC 50 for Rats: 2 Min. Exposure

by

I. Fuhr
E. H. Krackow

DECLASSIFIED
DOD DIR 5200.9

Forwarded to Chief, Chemical Warfare Service

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CYANOGEN CHLORIDE
LC 50 for Rats : 2 Min. Exposure

Project A 10.2 T.R.L.R. 27

ABSTRACT

OBJECT:

The object of project A 10.2 is to determine the toxicities of standard and proposed chemical warfare agents.

The object of the work described in this report was to determine the LC 50 of Cyanogen Chloride for rats exposed 2 min. and observed 15 days.

RESULTS:

The LC 50 of Cyanogen chloride has been determined. The following results were obtained:

Anal. Concn. mg./l.	Mortality fraction	%
4.2	0/12	0
5.8	0/12	0
5.9	3/12	25
7.5	4/12	33
11.2	6/12	50
13.2	8/12	67
15.6	11/12	92
16.3	12/12	100

CONCLUSIONS:

The LC 50 of cyanogen chloride for rats exposed for two minutes and observed for fifteen days is 10.1 mg./l. ($L(Ct)_{50}$ = 20,200).

RECOMMENDATIONS:

It is recommended that concentrations of CC be determined in field tests both by bioassay (rat) and by chemical analysis. It is believed that the rat would be useful particularly when the concentrations range between 6 and 15 mg./l.

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CYANOGEN CHLORIDE
LC 50 for Rats : 2 Min. Exposure

Project A 10.2 T.R.L.R. 27

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Project A 10.2 T.R.L.R. 27

I. INTRODUCTION.

A. Object.

The object of project A 10.2 is to determine the toxicities of standard and proposed chemical warfare agents.

The object of the work described in this report was to determine the LC 50 of cyanogen chloride for rats exposed 2 min. and observed 15 days.

B. Authority.

Work was done by authority of Chief, C.W.S., under project A 10.2.

II. HISTORICAL.

To date the LC 50 of cyanogen chloride for rats has not been reported. However, Marshall and Miller (PR 222) studied the toxicity of cyanogen chloride for the rat and several other species, varying either the time of exposure or the concentration of agent. From data collected on 65 rats, they found that, with death as the end point, the time-concentration relationship could be expressed as a smooth parabola becoming asymptotic to the axes. In these experiments the shortest exposure time was 7 1/2 minutes and the lethal concentration was found to be 0.89 mg./l.

These investigators described the symptoms as immediate excitement; irritation of the eyes and respiratory tract; lachrymation; salivation and an increased respiratory rate. These were followed by convulsions, prostration, unconsciousness, and death. In those animals surviving unconsciousness, recovery was fairly rapid and practically certain, depression lingering only for a day or two.

English investigators (Ph 1, XLVI.1, 1918) also observed the time-concentration relationship for the rat. At the two lowest exposure times they found the following:

Concn.	Exposure Time	Deaths
0.56 mg./l.	10 min.	0/2
1.40	10	3/3
1.40	5	2/8
2.80	5	2/2

III. EXPERIMENTAL.

A. Materials and Equipment.

Cyanogen chloride was obtained from the Protective Development Division, Technical Command, Edgewood Arsenal. It was 98% pure.

Rats were obtained from two sources, namely, Philadelphia Supply Co., Philadelphia, Pa., strain uncertain, and Medical Research Laboratory, Edgewood Arsenal, Wistar strain. All of the rats used weighed at least 200 g.

The 386-l. chamber described in E.A.T.R. 376 was used for gassing.

B. Procedure.

The large bubbler containing the cyanogen chloride was immersed in an ice bath during the gassings. Concentrations of the agent were set up in the chamber by passing nitrogen thru the bubbler. Twelve rats were exposed to each concentration. Alternate pairs of the two strains were placed in each of the six compartments. The animals were observed closely during and after each two minute exposure. The post-gassing observation period was 15 days.

Analytical concentrations were determined by absorbing the agent in 3% sodium hydroxide in 70% ethyl alcohol and analyzing for chloride by the Volhard technique.

C. Results.

1. Toxicity.

The following results were obtained:

Table 1

Toxicity of Cyanogen Chloride for Rats : 2 Min. Exposure

Anal. Concn. mg./l.	Room Temp. °C.	Rel. Hum. %	Mortality fraction	%
4.2	20	27	0/12	0
5.8	20	27	0/12	0
6.9	22	25	3/12*	25
7.5	20	22	4/12	33
11.2	20	21	6/12	50
13.2	20	22	8/12	67
15.6	22	25	11/12	92
16.3	21	21	12/12	100

*One of these three deaths occurred 10 days after exposure.

Data from Table 1 are plotted in Chart 1, which indicates that the LC 50 of cyanogen chloride for rats exposed 2 minutes and observed for 15 days is 10.1 mg./l. As already indicated, only one of the deaths was delayed. The remaining 43 deaths occurred within 40 minutes after gassing. There was relatively little difference in the mortality rate between the Wistar and the Philadelphia rats. Of the 44 rats killed, 57% were of the latter type.

2. Symptoms.

The rats became very active within a few seconds after being introduced into the chamber containing cyanogen chloride. They pawed continually at their noses and eyes and ran around wildly in their compartment. After approximately 30 seconds, the activity became violent, followed shortly thereafter by collapse, unconsciousness and death. Incapacitation and collapse occurred about 70 seconds after the start of exposure.

IV. DISCUSSION.

Comparisons between the LC 50 of CC for rats and goats, and the LC 50 for rats and goats are tabulated below:

Agent	Rat LC 50 mg./l.	Goat LC 50 mg./l.
CC	10.1	1.8 (TRLR 26)
AC	1.1 (TRLR 22)	1.1 (TRLR 23)

The wide difference between the LC 50 of CC for rats and goats is to be noted. Attempts at explanation may be based on two major premises, (1) differences in the ability of the two species to detoxicate, destroy or eliminate CC, and (2) differences in respiratory physiology.

Experiments have been performed recently by Lt. D. Karnofsky (unpublished) in which he found that the intravenous LD 50 of CC in rats and goats was about 6.0-6.5 mg./kg. and 3.0-3.5 mg./kg. respectively when injections made over a period of 1 minute. Unpublished data of the Biochemistry Section, Medical Research Laboratory, Edgewood Arsenal, have indicated that 30 second injections have established the LD 50 of CC for both dogs and rabbits at 3.0-3.5 mg./kg.

It thus appears that the LD 50 of CC for goats, rabbits and dogs is about the same, and presumably, the detoxication rates for CC are of the same magnitude. Since the LD 50 of CC for rats is about twice that for the other animals it may be assumed that the detoxication, destruction or elimination of CC proceeds at a higher rate for rats than for goats. However, this doubled detoxication rate cannot entirely explain the 6:1 ratio of the LC 50 by inhalation. This phenomenon must therefore be due to differences in the respiratory physiology of the two species. It is suggested that experiments be performed to show the effect of CC on the

amplitude and rate of respiration of rats and goats and clarify this point.

This resistance of the rat to cyanogen chloride is of particular interest in relation to field test studies in which it may be considered desirable to check analytical concentrations with animal data. Obviously, with higher concentrations of cyanogen chloride (6-15 mg./l.) rats could be used where goats and mice could not. Similarly, the converse of this is true at concentrations less than 6 mg./l.

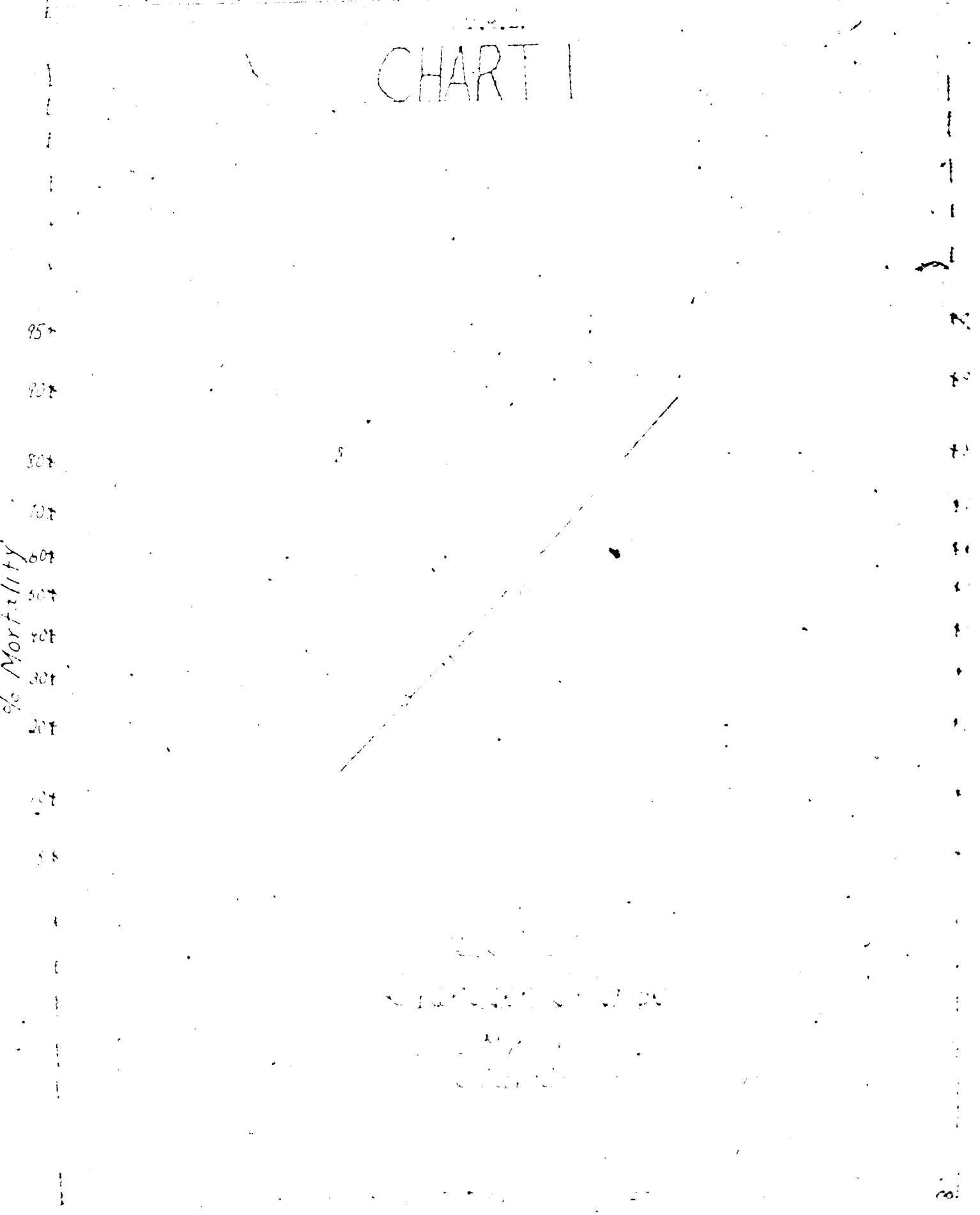
V. CONCLUSION.

The LC 50 of cyanogen chloride for rats exposed for two minutes and observed for fifteen days is 10.1 mg./l. (L(ct)50 = 20,200).

VI. RECOMMENDATIONS.

It is recommended that concentrations of CC be determined in field tests both by bioassay (rat) and by chemical analysis. It is believed that the rat would be useful particularly when the concentrations range between 6 and 15 mg./l.

CHART I



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CYANOGEN CHLORIDE
LC 50 for Rats : 2 Min. Exposure

Project A 10.2

Experimental Work:
Begun: 10 February 1944
Completed: 29 February 1944

Notebook: No. 1712

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Typed - 6 April 1944 - elr

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US ARMY RESEARCH, DEVELOPMENT AND ENGINEERING COMMAND
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5183 BLACKHAWK ROAD
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REPLY TO
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MEMORANDUM THRU Director, Edgewood Chemical Biological Center, (RDCB-D/Mr. Joseph Wienand), 5183 Blackhawk Road, Aberdeen Proving Ground, Maryland 21010-5424

FOR Defense Technical Information Center, 8725 John J. Kingman Road, Ft Belvoir, VA 22060

SUBJECT: Internal Request for Change in Distribution

1. This action is in response to an Edgewood Chemical Biological Center (ECBC) Internal Request for a Change in Distribution on documents related to cyanogen chloride.

2. The listed documents in the attachment have been reviewed by ECBC Subject Matter Experts and deemed suitable for the change in distribution to read "Approved for Public Release; distribution unlimited."

3. The point of contact is Adana L. Eilo, ECBC Security Specialist, (410) 436-2063, adana.l.eilo.civ@mail.mil.

Encl

MATTHEW A. SPAULDING
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Cyanogen Chloride References

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[5] Kolls, AC, Kuhn, HA, and Todd, AJ, *Report on Toxicity Tests on Mice*, **Report No. 33** in Marshall, EK ed., **Pharmacological and Research Section Monographs**. War Department Chemical Warfare Service, Research Division, American University Experiment Station, Washington, DC, c. 1917. On file with the Historical Research and Response Team, Research, Development and Engineering Command, Aberdeen Proving Ground, MD. Unclassified, Dist. E, DoD Only.

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